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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Yoshio Umezawa

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07/21/2009

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EXAMINER

BURKHART, MICHAEL D

ART UNIT

PAPER NUMBER

1633

MAIL DATE

DELIVERY MODE

07/21/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/501,947	Applicant(s) UMEZAWA ET AL.	
	Examiner Michael Burkhart	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 3/13/2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5,7,9-14,21 and 22 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5,7,9-14,21 and 22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Receipt and entry of the amendment dated 3/13/2009 is acknowledged. After entry of the amendment, claims 1-5, 7, 9-14, 21 and 22 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Terminal Disclaimer

The terminal disclaimer filed on 6/24/2008 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of 7,166,447 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 103

Claims 1-5, 7, 9-14, 21, and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Umezawa et al (WO 02/08766, 1/31/2002, of record) in view of Ozawa et al (Anal. Chem., 2001, of record), Hamilton et al (U.S. 6,780,599, of record), Simpson et al (EMBO reports, 2000, of record), and Martoglio et al (TICB, 1998, of record). **This rejection is maintained for reasons made of record in the Office Actions dated 5/15/2007, 2/25/2008, 11/13/2008, and for reasons set forth below.**

Claim 1 has been amended to recite that a fluorescent signal is generated only when the fusion proteins are located within the same organelle. Such a limitation is considered to be taught by the totality of the art of record, for reasons set forth in the previous Office Actions.

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For example, Ozawa et al teach a method for analyzing protein interactions in eukaryotic cells using a split-luciferase system, which may include evaluating organelle-associated proteins (page 2521, end of the second column). Hamilton et al teach fragments of fluorescent proteins for a protein fragment complementation assay, which can be used with a targeting peptide fused to the fusion proteins in order to localize the fusion proteins to a subcellular compartment (column 16, lines 7-19). Taken together, the teachings of the totality of the prior art require that the two fusion proteins be in close proximity in order for protein splicing to take place. Thus, the skilled artisan would realize that the two fusion proteins would have to be located in the same organelle in order for fluorescence to occur.

Response to Arguments

Applicant's arguments filed 3/13/2009 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) the organelle targeting peptide (OTS) of fusion peptide (a) and the test protein (b) of the instant invention do not directly interact, in contrast to the teachings of the prior art; 2) Umezawa et al is directed to protein-protein interaction analysis whereas the claimed methods do not have such an interaction, instead, they rely upon confinement of the fusion proteins to the organelle in order to bring the inteins into close proximity, which is not taught by Umezawa et al; 3) Ozawa and Hamilton et al are directed to protein-protein interaction analysis whereas the claimed methods do not have such an interaction, instead, they rely upon confinement of the fusion proteins to the organelle in order to bring the inteins into close proximity, which is not taught by Ozawa or Hamilton et al; 4) neither Simpson nor Martoglio et al remedy these deficiencies.

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Regarding 1), this is not a limitation of claims 5, 7, 9-14, 21, or 22. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., indirect interaction between the fusion proteins) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicants present no further arguments regarding these claims, hence, the rejections stands.

Further regarding 1), amended claim 1 recites that the test protein does not directly interact with the OTS of the fusion peptide (a), not that the fusion peptides (a) and (b) themselves do not interact. The teachings of Umezawa, Ozawa, Hamilton, Simpson and Martoglio et al do not require or suggest such an interaction. A review of the previous Office Actions does not reveal the Examiner has ever suggested this to be a part of the logic or reasoning behind the rejection. Rather, it is the interaction between the intein half-peptides that is crucial to the methods of the prior art and of the instant invention. See for example, Figs. 1 and 2 of Ozawa et al and Fig. 1 of the instant invention. The OTS peptide is only required to direct fusion peptide (a) to the organelle of choice, there is no requirement or teachings of the OTS mediating the direct interaction of the fusion peptides (a) and (b). There are no teachings that the test protein must interact with the OTS of fusion peptide (a), rather it is suggested that the intein half-peptides will interact once they are localized to the same organelle. Furthermore, the structure of the components and method steps of the prior art are no different from those instantly claimed, and thus, any inherent properties of the claimed fusion peptides would also be found in the fusion peptides taught by the prior art. Finally, it is noted that the interaction of the fusion

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peptides is not a step under control of applicants or the skilled artisan, it is a function of, and controlled by, the structure of the fusion peptides and the cells they are localized in. Thus, any teachings of the claimed fusion peptides would also be a teaching of any inherent properties these fusion peptides might have, e.g. the OTS not interacting with the test protein, or protein splicing occurring in close proximity.

Regarding 2) and 3), a review of the instant application reveals no instances wherein a protein splicing event (and therefore a fluorescent signal is generated) occurs without protein-protein interaction. Applicants working example uses the interaction between DnaEn and DnaEc (e.g. Fig. 10 even has this interaction spelled out) in the mitochondria. It is therefore unclear how this argument mitigates against the instant rejection, as "protein-protein interactions" are not excluded by the claim language (see below). It is further noted that the instant disclosure does not present any evidence or working examples that intein-mediated protein splicing can occur in the absence of protein-protein interaction. The instant application could therefore not have solved any problems that might occur when attempting to perform such a splicing of protein domains, and did not advance the art of doing so in any meaningful way.

Further regarding 2) and 3), In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., the inteins are brought into close proximity by confinement to the same organelle, intein splicing occurs without protein-protein interaction) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

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Regarding 4), the Umezawa, Ozawa, and Hamilton et al references are not deemed to have any deficiencies for reasons set forth above.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Burkhart whose telephone number is (571)272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael Burkhart/
Primary Examiner, Art Unit 1633